

Dear supporters, partners, patients and parents,

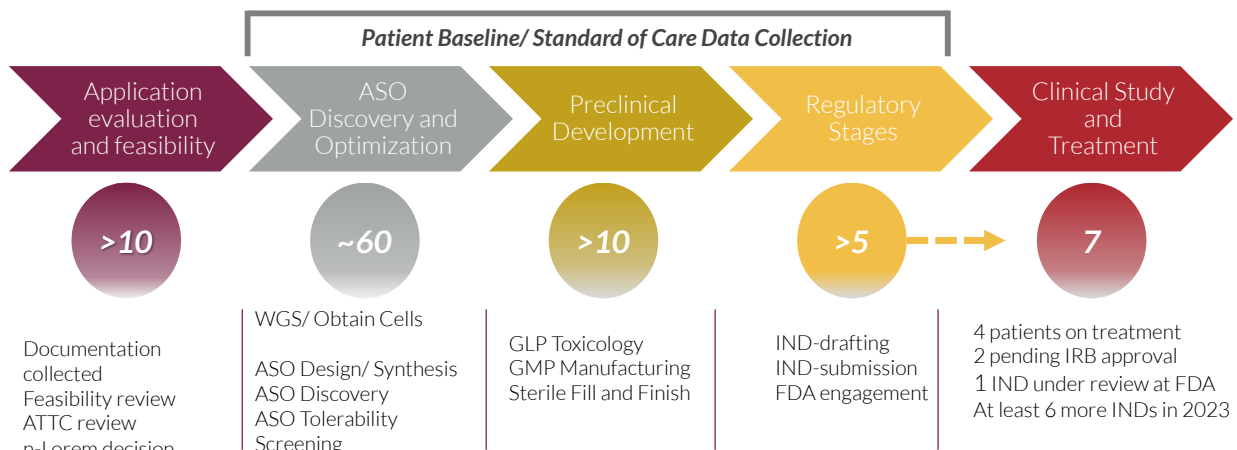
As we enter the second half of 2023, I hope to take a moment of your time to thank you on behalf of our patients for your wonderful generosity and to provide a summary of all that we have accomplished in three and a half years. I am proud of what we have accomplished but know that the need is so great that we must re-double our efforts to meet the needs of the nano-rare community.

Treating patients in need today

Because the demand continues to increase, despite all the resources we have added, we are still not able to get treatments to patients as rapidly as we would like. We have now processed applications for the treatment of more than 200 patients and accepted about 100 patients for treatment. Our current pipeline of hope and potential help represents an extraordinary achievement of a tiny group of committed, caring professionals. To have filed seven investigational new drug applications (INDs) with the FDA in so little time with such a small organization is a stunning achievement. Each of these INDs represents a needy patient and a desperate family. Importantly, we have had INDs approved by three different divisions of the FDA, meaning that patients with diseases in the brain, the eye and the kidney are potential beneficiaries.

Our pipeline shows that we are advancing patient programs across all areas of discovery and development.

> 90 Patient Programs in Development
Expect at least 10 INDs in 2023



Evidence of benefit

Given how advanced the diseases are of most of our patients, I worried that we might not be able to provide meaningful benefit to any patient. Well, I no longer worry about that. The experience with Anna and, most recently, Susannah give us a resoundingly positive **YES** to the question if patients with advanced diseases can be helped. This is great news for all patients and Anna and Susannah are true pioneers showing the way for patients to be treated with personalized ASOs. To have such clear observations of help so soon is deeply rewarding to all of us involved in this effort and provides hope to those awaiting treatment.

Nano-rare patients deserve quality at every critical step leading to treatment

I am pleased to report that the quality systems we implemented on day one are doing the job they were designed to do. From the moment we receive a patient's application, we understand that we have a patient's well-being in our hands. We are delivering quality, especially the all-important steps of assuring that each patient is treated with an optimal ASO that only exposes the patient to prudent risk.

Health care equity

In a developed economy, I believe access to quality health care is a right, and at n-Lorem, we do our best for every single patient every single day. We do take what we call 'directed donations' from groups and individuals interested in supporting research on a particular gene or mutation. These directed donations support and expand our infrastructure, which supports the treatment of all patients. For each directed donation, we request a donation to our general fund to accomplish this. Importantly, what we learn from research on one gene informs what we know about all nano-rare mutations. It is impossible to overemphasize the long-term value of what we learn from each gene we study and each patient we treat. Long term, I am confident that what we are learning will benefit all humans.

Meeting the demand

Most importantly, we have expanded to try to meet the overwhelming demand. As our new lab comes online, we will more than triple our ASO discovery capacity. Our ability to build, equip and staff our new lab happened years earlier than planned because of your generosity, our supporters.



But a lab is a shell and what makes it exciting and productive is the quality and commitment of the team in the lab. I am thrilled with the team of dedicated scientists we employ at Ionis and La Jolla Lab and those who have joined us in our El Cajon laboratory (pictured below).

**Principal Scientist,
Neurological Drug Discovery**



Ram

Senior Scientists





Julia Ria Wei

Scientists








Ana Elena Lesley Swappi

Building a senior team that nano-rare patients can count on


I have been running organizations for many years and can state with confidence that the senior team at n-Lorem is the best team I have had the privilege to lead. We are all united by our mission and we believe that all patients matter. No patient should be left behind. The senior team is now supported by an equally capable more junior team.




**Stanley T. Crooke,
M.D., Ph.D.**
*Founder, Chairman, and
CEO*




**C. Frank Bennett,
Ph.D.**
Chief Technical Officer




Sarah Glass, Ph.D.
Chief Operating Officer




Joe Gleeson, M.D.
Chief Medical Officer




**Julie Douville,
Ph.D.**
*Exec. Director, ASO
Discovery and
Development*




Kim Butler
*Sr. Director of
Operations*




**Jeff Carroll,
Ph.D.**
Scientific Advisor



**Laurence Mignon,
Ph.D.**
*Sr. Director of
Clinical
Development*



**Cedrik Ngongang,
M.D.**
*Sr. Director, Medical
Geneticist*



**Amy C. Williford,
Ph.D.**
*Sr. Director of
Communications
and Donor Relations*

Sharing what we learn

We must share what we learn as broadly as possible. At n-Lorem, we have already published 8 peer-reviewed manuscripts in high-impact journals. In the latest paper in Nature Biotechnology, we describe the plight of a single one of our patients, then lay out the reforms so desperately needed, and will be submitting additional publications this fall. I am absolutely certain that these reforms are not only affordable but will reduce the cost of health care over time. We need every one of you to put your shoulder to the wheel here and help us drive the reforms through state and national governments and the insurers who you pay every day for your health care insurance. Make all of these folks listen and join us in this effort that will help all patients.

On October 12, we will welcome all to our first n-Lorem Nano-rare Patient Colloquium, a collection of patients, partners and physicians. We are tremendously excited to have the opportunity to share what we have accomplished what we have learned and the challenges we face with all interested parties. We look forward to seeing you there. Our wonderful donor and partner, Biogen, is hosting this gathering and I am excited to tell you that Biogen's CEO, Chris Viehbacher will join us to express his commitment to nano-rare patients.

Creating a community

I am thrilled with the response to our Patient Empowerment Program. If you haven't listened to both the interviews and the informative lectures in our podcast series, I hope you do. I think you will enjoy them, learn from them and emote with others who suffer from nano-rare mutations.

We can do this!

I was told that helping nano-rare patients today was impossible. Thanks to your support, I can say that it CAN BE DONE TODAY, and with your help, we will do more tomorrow.

Gratefully,

A handwritten signature in black ink, appearing to read "Stanley T. Crooke". The signature is fluid and cursive, with a long horizontal stroke at the end.

Stanley T. Crooke, M.D., Ph.D.

